

CAS ONLINE PRINTOUT 09/698,071

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(FILE 'HOME' ENTERED AT 07:20:14 ON 11 SEP 2002)

FILE 'REGISTRY' ENTERED AT 07:20:37 ON 11 SEP 2002

L1 STRUCTURE uploaded
L2 1 S L1
L3 56 S L1 FUL
L4 STRUCTURE uploaded
L5 0 S L4
L6 13 SEARCH L4 SSS SUB=L3 FULL

FILE 'CAPLUS' ENTERED AT 07:23:53 ON 11 SEP 2002

L7 8 S L6

FILE 'REGISTRY' ENTERED AT 07:37:28 ON 11 SEP 2002

L8 STRUCTURE uploaded
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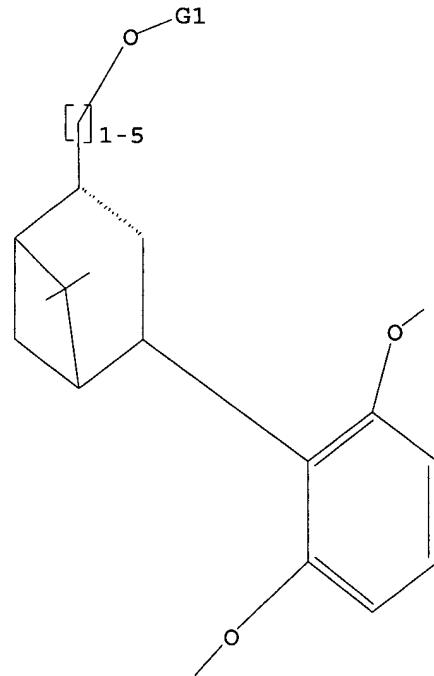
FILE 'CAPLUS' ENTERED AT 07:38:31 ON 11 SEP 2002

L10 4 S L9

=> d 18

L8 HAS NO ANSWERS

L8 STR



G1 Me,Et,n-Pr,i-Pr,H

Structure attributes must be viewed using STN Express query preparation.

=> d bib abs hitstr 1-4

L10 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2001:338346 CAPLUS
DN 134:348297

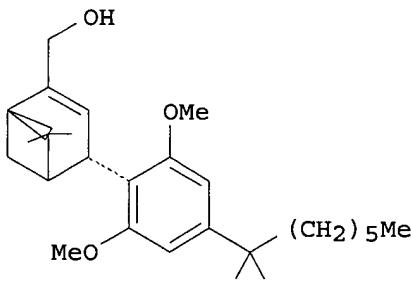
TI 4-Phenyl pinene derivatives as agonists specific for the peripheral cannabinoid receptor and their therapeutic uses
 IN Fride, Ester; Breuer, Aviva; Hanus, Lumir; Tchilibon, Susanna; Horowitz, Michal; Mechoulam, Raphael; Garzon, Aaron
 PA Yissum Research Development Company of the Hebrew University, Israel
 SO PCT Int. Appl., 43 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001032169	A1	20010510	WO 2000-US29903	20001030
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRAI IL 1999-132661 A 19991031

OS MARPAT 134:348297

GI



AB The invention provides novel pharmaceutical compns. comprising as the active ingredient 4-Ph pinene derivs. which are specific for the peripheral cannabinoid receptors. In particular, the compds. of the invention bind efficiently to CB2 but do not bind to CB1. The compds. show no activity in behavioral tests in mice which together have been shown to be specific for tetrahydrocannabinol (THC)- type activity in the central nervous system mediated by CB1 but reduce blood pressure, block intestinal mobility, and elicit anti-inflammatory and peripheral analgetic activity. The invention also relates to methods of treating, preventing, or managing hypertension, inflammation, pain, gastrointestinal diseases, autoimmune diseases, and tumors with the compds. of the invention. HU-308 (I) (prepn. given) at 10 and 20 mg/kg, administer i.p. to mice daily for seven days, reduced the severity of acid-induced inflammatory bowel disease.

IT 256934-39-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid

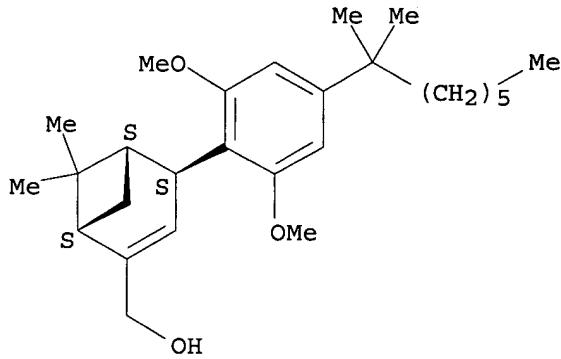
CAS ONLINE PRINTOUT 09/698,071

receptor and therapeutic uses)

RN 256934-39-1 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



IT 338971-67-8P

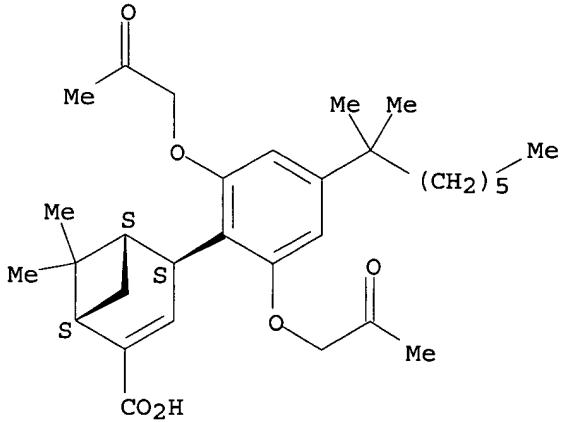
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid receptor and therapeutic uses)

RN 338971-67-8 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[4-(1,1-dimethylheptyl)-2,6-bis(2-oxopropoxy)phenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



IT 338971-68-9P

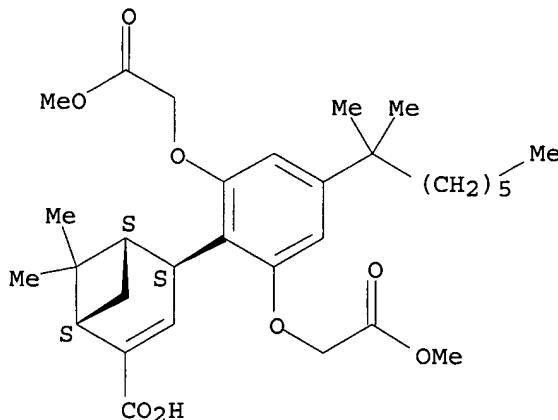
RL: SPN (Synthetic preparation); PREP (Preparation)

(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid receptor and therapeutic uses)

RN 338971-68-9 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[4-(1,1-dimethylheptyl)-2,6-bis(2-methoxy-2-oxoethoxy)phenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

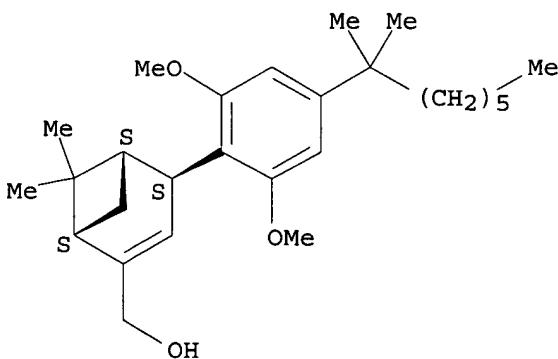
Rotation (+). Absolute stereochemistry unknown.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
 AN 2000:614228 CAPLUS
 DN 133:260976
 TI Looking back at cannabis research
 AU Mechoulam, Raphael
 CS Medical Faculty, Department of Medicinal Chemistry and Natural Products, Hebrew University, Jerusalem, 91120, Israel
 SO Current Pharmaceutical Design (2000), 6(13), 1313-1322
 CODEN: CPDEFP; ISSN: 1381-6128
 PB Bentham Science Publishers
 DT Journal; General Review
 LA English
 AB A review with 70 refs. Research leading to the isolation of the plant cannabinoids during the 1960's and to the endogenous cannabinoids, during the 1990's is described. Investigations on two non-psychotropic, synthetic cannabinoids, HU-211, a neuroprotective agent and HU-308, a specific CB2 agonist are presented.
 IT 256934-39-1, HU 308
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (looking back at cannabis research)
 RN 256934-39-1 CAPLUS
 CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

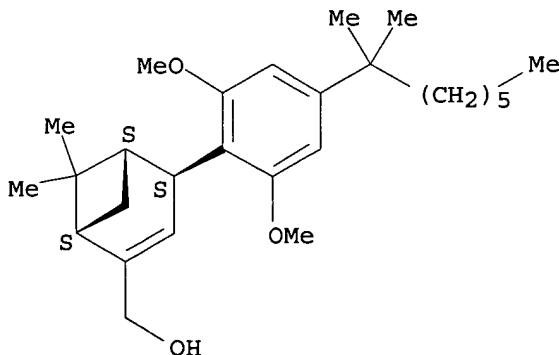
Rotation (+). Absolute stereochemistry unknown.



RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
 AN 1999:796665 CAPLUS
 DN 132:132238
 TI HU-308: a specific agonist for CB2, a peripheral cannabinoid receptor
 AU Hanus, L.; Breuer, A.; Tchilibon, S.; Shiloah, S.; Goldenberg, D.;
 Horowitz, M.; Pertwee, R. G.; Ross, R. A.; Mechoulam, R.; Fride, E.
 CS Department of Medicinal Chemistry and Natural Products, Medical Faculty,
 Hebrew University, Jerusalem, 91120, Israel
 SO Proceedings of the National Academy of Sciences of the United States of
 America (1999), 96(25), 14228-14233
 CODEN: PNASA6; ISSN: 0027-8424
 PB National Academy of Sciences
 DT Journal
 LA English
 AB Two cannabinoid receptors have been identified: CB1, present in the
 central nervous system (CNS) and to a lesser extent in other tissues, and
 CB2, present outside the CNS, in peripheral organs. There is evidence for
 the presence of CB2-like receptors in peripheral nerve terminals. We
 report now that we have synthesized a CB2-specific agonist, code-named
 HU-308. This cannabinoid does not bind to CB1 ($K_i > 10 \mu M$), but does
 so efficiently to CB2 ($K_i = 22.7 \pm 3.9 \text{ nM}$); it inhibits
 forskolin-stimulated cAMP prodn. in CB2-transfected cells, but does so
 much less in CB1-transfected cells. HU-308 shows no activity in mice in a
 tetrad of behavioral tests, which together have been shown to be specific
 for tetrahydrocannabinol (THC)-type activity in the CNS mediated by CB1.
 However, HU-308 reduces blood pressure, blocks defecation, and elicits
 anti-inflammatory and peripheral analgesic activity. The hypotension, the
 inhibition of defecation, the anti-inflammatory and peripheral analgesic
 effects produced by HU-308 are blocked (or partially blocked) by the CB2
 antagonist SR-144528, but not by the CB1 antagonist SR-141716A. These
 results demonstrate the feasibility of discovering novel nonpsychotropic
 cannabinoids that may lead to new therapies for hypertension,
 inflammation, and pain.
 IT 256934-39-1P, HU 308
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
 effector, except adverse); BPR (Biological process); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological
 study); PREP (Preparation); PROC (Process)
 (HU-308: a specific agonist for CB2, a peripheral cannabinoid receptor)
 RN 256934-39-1 CAPLUS
 CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-
 dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

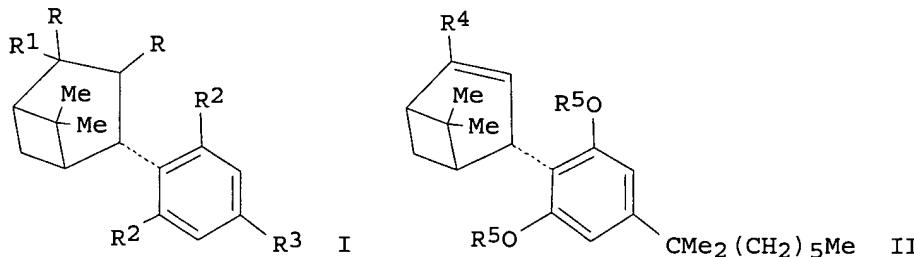
Rotation (+). Absolute stereochemistry unknown.



RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1995:759141 CAPLUS
DN 123:314212
TI Preparation and neuroprotective pharmaceutical compositions of
4-phenylpinene derivatives
IN Mechoulam, Raphael; Breuer, Aviva; Biegon, Anat
PA Yissum Research Development Co., USA; Pharmos Corp.
SO U.S., 24 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5434295 IL 112558	A A1	19950718 20000726	US 1994-192924 IL 1995-112558	19940200 19950200
PRAI	US 1994-192924	A	19940207		
OS	MARPAT 123:314212				
GI					



AB The title compds. I (R = H, R2 = bond; R1 = a variety of org. moieties; R2 = alkyl, halo, various oxy groups; R3 = alkyl groups, ether groups, or combinations thereof) were prep'd. as active ingredients of pharmaceutical compns. displaying neuroprotectant and antiglaucoma effects. Thus, 4-hydroxymyrtanyl pivalate was treated with 5-(1,1-dimethylheptyl)resorcinol to give the title deriv. II (R4 = $\text{CH}_2\text{O}_2\text{CCMe}_3$, R5 = H), which was converted to II (R = CO₂H, R1 = Ac) (III) in several steps. At 1 μM III blocked the NMDA response at the glutamate receptor by 35%. III caused a significant redn. in intraocular pressure in rabbits which indicated a possible therapeutic use in glaucoma treatment.

IT 169287-91-6P 169287-93-8P

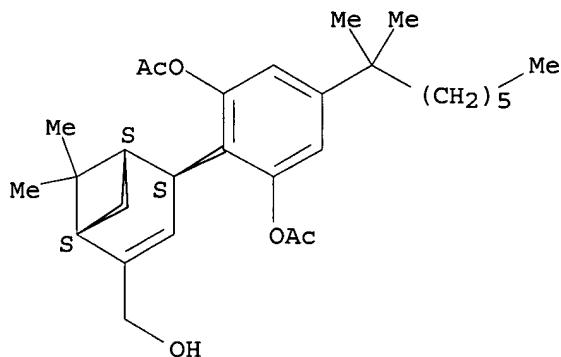
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and neuroprotective pharmaceutical comps. of 4-phenylpinene derivs.)

RN 169287-91-6 CAPLUS

CN 1,3-Benzenediol, 5-(1,1-dimethylheptyl)-2-[4-(hydroxymethyl)-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-, 1,3-diacetate, [1S-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

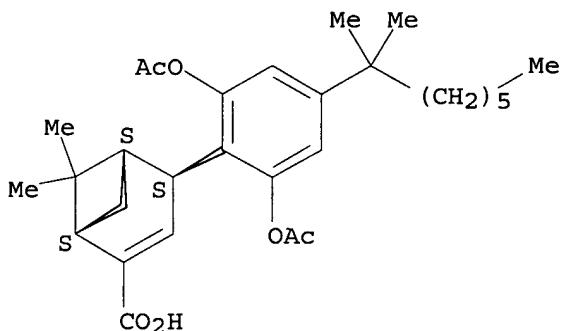
Absolute stereochemistry. Rotation (+).



RN 169287-93-8 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[2,6-bis(acetyloxy)-4-(1,1-dimethylheptyl)phenyl]-6,6-dimethyl-, [1S-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 169287-98-3P

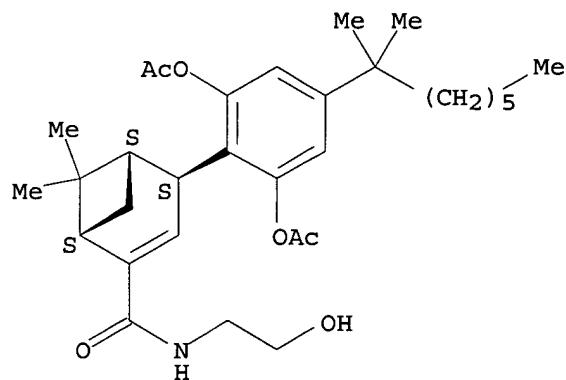
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and neuroprotective pharmaceutical compns. of 4-phenylpinene derivs.)

RN 169287-98-3 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-carboxamide, 4-[2,6-bis(acetyloxy)-4-(1,1-dimethylheptyl)phenyl]-N-(2-hydroxyethyl)-6,6-dimethyl-, [1S-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

CAS ONLINE PRINTOUT 09/698,071



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CAS ONLINE PRINTOUT 09/698,071

=> d his

(FILE 'HOME' ENTERED AT 07:20:14 ON 11 SEP 2002)

FILE 'REGISTRY' ENTERED AT 07:20:37 ON 11 SEP 2002

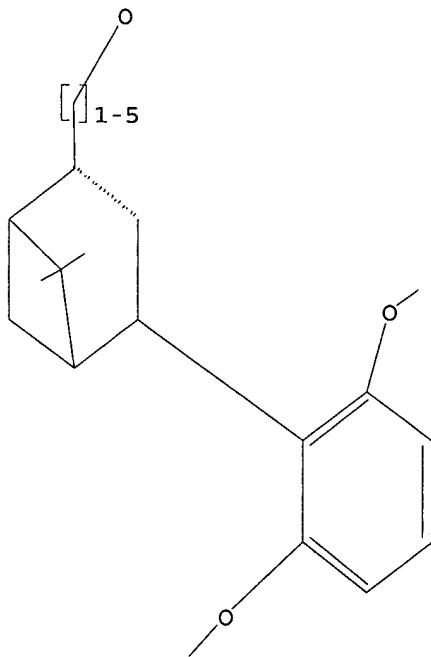
L1 STRUCTURE uploaded
L2 1 S L1
L3 56 S L1 FUL
L4 STRUCTURE uploaded
L5 0 S L4
L6 13 SEARCH L4 SSS SUB=L3 FULL

FILE 'CAPLUS' ENTERED AT 07:23:53 ON 11 SEP 2002

L7 8 S L6

=> d 14

L4 HAS NO ANSWERS
L4 STR



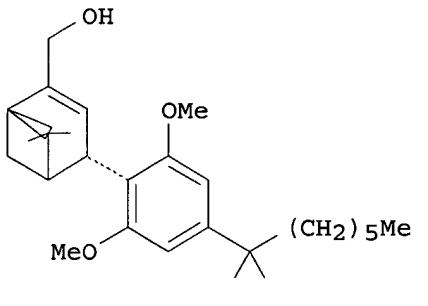
Structure attributes must be viewed using STN Express query preparation.

=> d bib abs hitstr 1-8

L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2001:338346 CAPLUS
DN 134:348297
TI 4-Phenyl pinene derivatives as agonists specific for the peripheral cannabinoid receptor and their therapeutic uses
IN Fride, Ester; Breuer, Aviva; Hanus, Lumir; Tchilibon, Susanna; Horowitz, Michal; Mechoulam, Raphael; Garzon, Aaron
PA Yissum Research Development Company of the Hebrew University, Israel
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001032169	A1	20010510	WO 2000-US29903	20001030
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	IL 1999-132661	A	19991031		
OS	MARPAT 134:348297				
GI					



AB The invention provides novel pharmaceutical compns. comprising as the active ingredient 4-Ph pinene derivs. which are specific for the peripheral cannabinoid receptors. In particular, the compds. of the invention bind efficiently to CB2 but do not bind to CB1. The compds. show no activity in behavioral tests in mice which together have been shown to be specific for tetrahydrocannabinol (THC)- type activity in the central nervous system mediated by CB1 but reduce blood pressure, block intestinal mobility, and elicit anti-inflammatory and peripheral analgetic activity. The invention also relates to methods of treating, preventing, or managing hypertension, inflammation, pain, gastrointestinal diseases, autoimmune diseases, and tumors with the compds. of the invention. HU-308 (I) (prepn. given) at 10 and 20 mg/kg, administer i.p. to mice daily for seven days, reduced the severity of acid-induced inflammatory bowel disease.

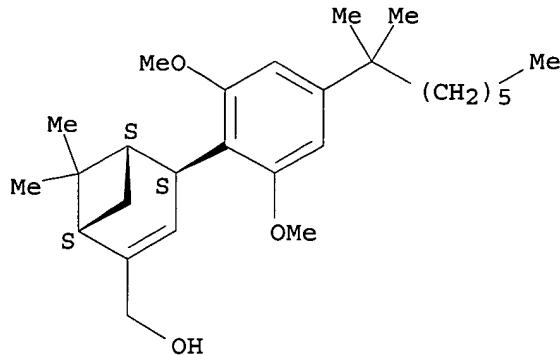
IT 256934-39-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid receptor and therapeutic uses)

RN 256934-39-1 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



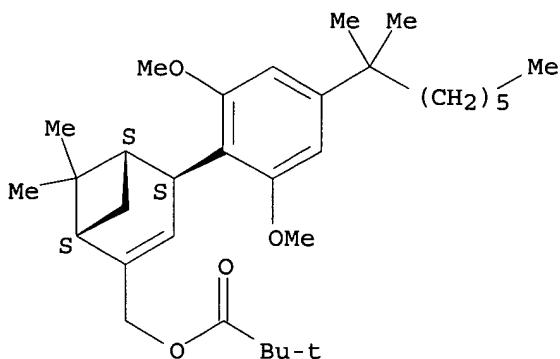
IT 256665-46-0P 338971-67-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (4-Ph pinene derivs. as agonists specific for peripheral cannabinoid receptor and therapeutic uses)

RN 256665-46-0 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [(1R,4R,5R)-4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester, rel- (9CI) (CA INDEX NAME)

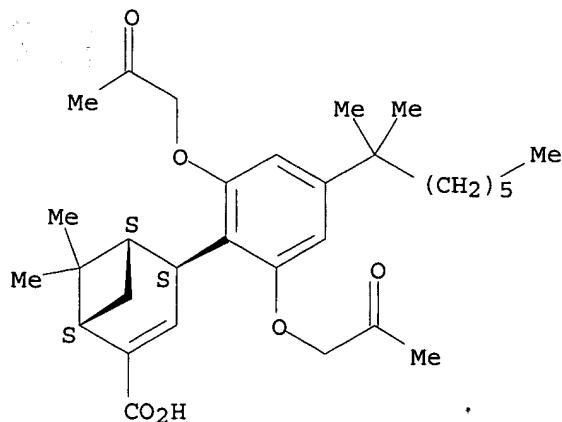
Relative stereochemistry.



RN 338971-67-8 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[4-(1,1-dimethylheptyl)-2,6-bis(2-oxopropoxy)phenyl]-6,6-dimethyl-, (1R,4R,5R)-rel- (+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



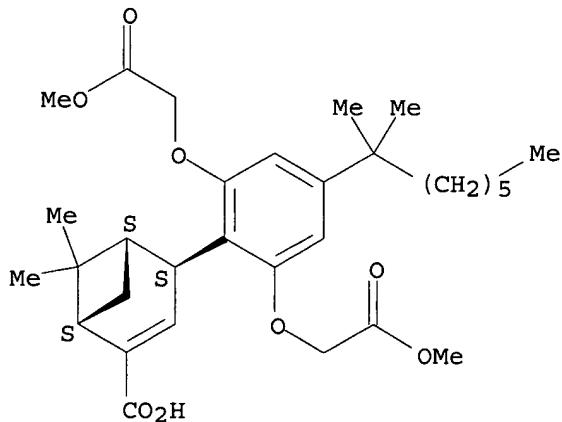
IT 338971-68-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid receptor and therapeutic uses)

RN 338971-68-9 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[4-(1,1-dimethylheptyl)-2,6-bis(2-methoxy-2-oxoethoxy)phenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 2000:614228 CAPLUS

DN 133:260976

TI Looking back at cannabis research

AU Mechoulam, Raphael

CS Medical Faculty, Department of Medicinal Chemistry and Natural Products, Hebrew University, Jerusalem, 91120, Israel

SO Current Pharmaceutical Design (2000), 6(13), 1313-1322
CODEN: CPDEFP; ISSN: 1381-6128

PB Bentham Science Publishers

DT Journal; General Review

LA English

AB A review with 70 refs. Research leading to the isolation of the plant cannabinoids during the 1960's and to the endogenous cannabinoids, during

the 1990's is described. Investigations on two non-psychotropic, synthetic cannabinoids, HU-211, a neuroprotective agent and HU-308, a specific CB2 agonist are presented.

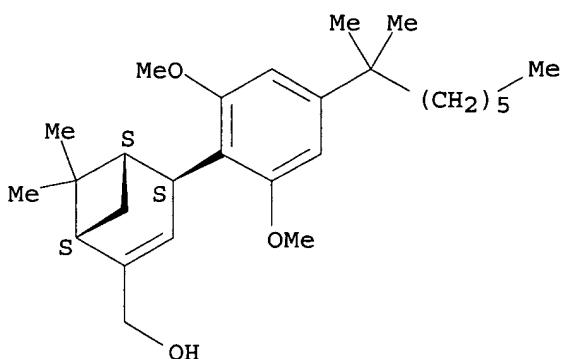
IT 256934-39-1, HU 308

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(looking back at cannabis research)

RN 256934-39-1 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 1999:796665 CAPLUS

DN 132:132238

TI HU-308: a specific agonist for CB2, a peripheral cannabinoid receptor

AU Hanus, L.; Breuer, A.; Tchilibon, S.; Shiloah, S.; Goldenberg, D.; Horowitz, M.; Pertwee, R. G.; Ross, R. A.; Mechoulam, R.; Fride, E.

CS Department of Medicinal Chemistry and Natural Products, Medical Faculty, Hebrew University, Jerusalem, 91120, Israel

SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(25), 14228-14233

CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB Two cannabinoid receptors have been identified: CB1, present in the central nervous system (CNS) and to a lesser extent in other tissues, and CB2, present outside the CNS, in peripheral organs. There is evidence for the presence of CB2-like receptors in peripheral nerve terminals. We report now that we have synthesized a CB2-specific agonist, code-named HU-308. This cannabinoid does not bind to CB1 ($K_i > 10 \mu M$), but does so efficiently to CB2 ($K_i = 22.7 \pm 3.9 \text{ nM}$); it inhibits forskolin-stimulated cAMP prodn. in CB2-transfected cells, but does so much less in CB1-transfected cells. HU-308 shows no activity in mice in a tetrad of behavioral tests, which together have been shown to be specific for tetrahydrocannabinol (THC)-type activity in the CNS mediated by CB1. However, HU-308 reduces blood pressure, blocks defecation, and elicits anti-inflammatory and peripheral analgesic activity. The hypotension, the inhibition of defecation, the anti-inflammatory and peripheral analgesic effects produced by HU-308 are blocked (or partially blocked) by the CB2 antagonist SR-144528, but not by the CB1 antagonist SR-141716A. These results demonstrate the feasibility of discovering novel nonpsychotropic

cannabinoids that may lead to new therapies for hypertension, inflammation, and pain.

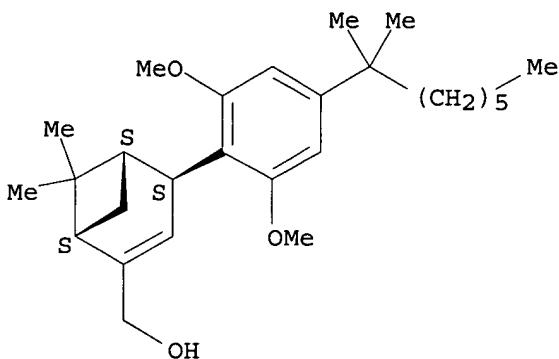
IT 256934-39-1P, HU 308

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(HU-308: a specific agonist for CB2, a peripheral cannabinoid receptor)

RN 256934-39-1 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel- (+) - (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



IT 256665-46-0P

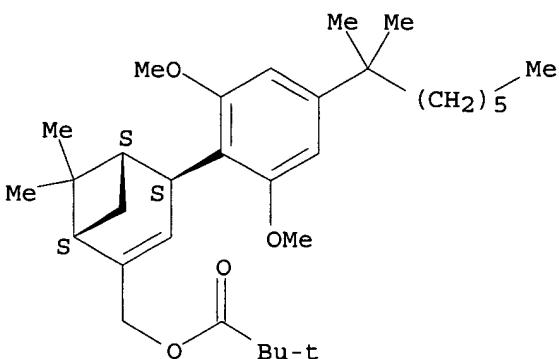
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(HU-308: a specific agonist for CB2, a peripheral cannabinoid receptor)

RN 256665-46-0 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [(1R,4R,5R)-4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 1995:759141 CAPLUS

DN 123:314212

TI Preparation and neuroprotective pharmaceutical compositions of

4-phenylpinene derivatives

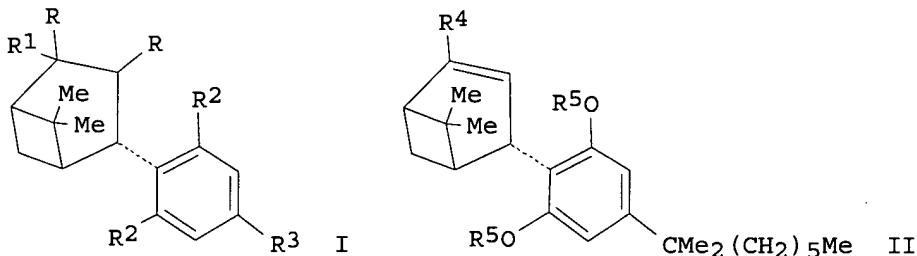
IN Mechoulam, Raphael; Breuer, Aviva; Biegon, Anat
 PA Yissum Research Development Co., USA; Pharmos Corp.

SO U.S., 24 pp.
 CODEN: USXXAM

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5434295 IL 112558	A A1	19950718 20000726	US 1994-192924 IL 1995-112558	19940207 19950206
PRAI	US 1994-192924	A	19940207		
OS	MARPAT 123:314212				
GI					

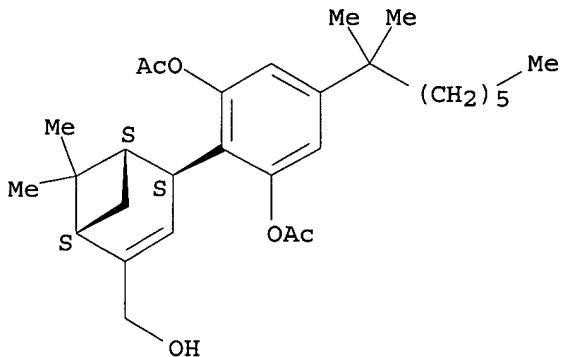


AB The title compds. I (R = H, R2 = bond; R1 = a variety of org. moieties; R2 = alkyl, halo, various oxy groups; R3 = alkyl groups, ether groups, or combinations thereof) were prep'd. as active ingredients of pharmaceutical compns. displaying neuroprotectant and antiglaucoma effects. Thus, 4-hydroxymyrtanyl pivalate was treated with 5-(1,1-dimethylheptyl)resorcinol to give the title deriv. II (R4 = CH2O2CCMe3, R5 = H), which was converted to II (R = CO2H, R1 = Ac) (III) in several steps. At 1 .mu.M III blocked the NMDA response at the glutamate receptor by 35%. III caused a significant redn. in intraocular pressure in rabbits which indicated a possible therapeutic use in glaucoma treatment.

IT 169287-91-6P 169287-93-8P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. and neuroprotective pharmaceutical compns. of 4-phenylpinene derivs.)

RN 169287-91-6 CAPLUS
 CN 1,3-Benzenediol, 5-(1,1-dimethylheptyl)-2-[4-(hydroxymethyl)-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-, 1,3-diacetate, [1S-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

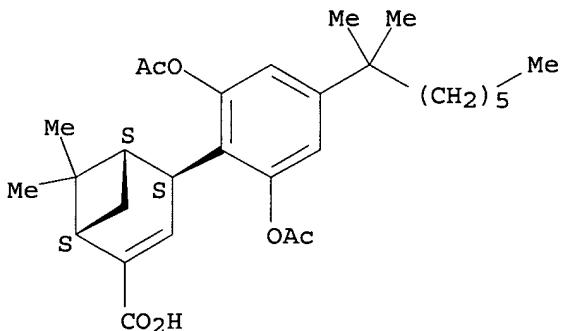
Absolute stereochemistry. Rotation (+).



RN 169287-93-8 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[2,6-bis(acetyloxy)-4-(1,1-dimethylheptyl)phenyl]-6,6-dimethyl-, [1S-(1. α ,4. α ,5. α .)]- (9CI) (CA INDEX NAME)

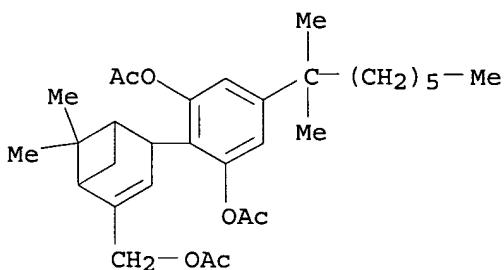
Absolute stereochemistry. Rotation (+).



IT 76163-87-6P, HU 254 169287-98-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and neuroprotective pharmaceutical compns. of 4-phenylpinene derivs.)

RN 76163-87-6 CAPLUS

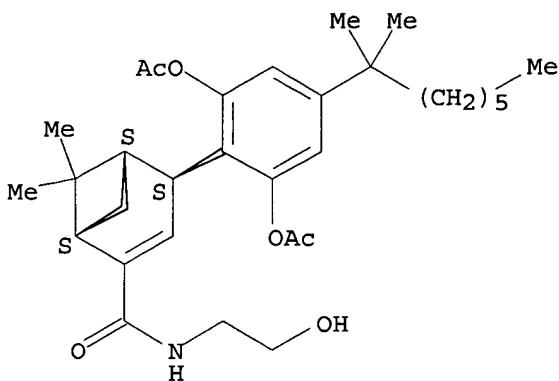
CN 1,3-Benzene diol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1S-(1. α ,2. α ,5. α .)]- (9CI) (CA INDEX NAME)

RN 169287-98-3 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-carboxamide, 4-[2,6-bis(acetyloxy)-4-(1,1-

dimethylheptyl)phenyl]-N-(2-hydroxyethyl)-6,6-dimethyl-,
 [1S-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
 AN 1993:246926 CAPLUS

DN 118:246926

TI Discriminative stimulus effects and receptor binding of enantiomeric pairs of cannabinoids in rats and pigeons; a comparison

AU Jaerbe, Torbjorn U. C.; Hiltunen, Arto J.; Mathis, Diane A.; Hanus, Lumir; Breuer, Aviva; Mechoulam, Raphael

CS Fac. Soc. Sci., Univ. Uppsala, Uppsala, S-751 48, Swed.

SO J. Pharmacol. Exp. Ther. (1993), 264(2), 561-9
 CODEN: JPETAB; ISSN: 0022-3565

DT Journal

LA English

AB The cannabimimetic activity of two enantiomeric pairs of compds. structurally different from the classical cannabinoids was evaluated in rats and pigeons, trained to discriminate between the presence and absence of (-)-.DELTA.-9-tetrahydrocannabinol (THC). One pair of enantiomers [compds. (+)-HU-249 and (-)-HU-250] has a 5-membered oxygen-contg. benzofuran ring; the second pair [(+)-HU-253 and (-)-HU-254] does not have an oxygen-contg. ring. The onset of cannabimimetic activity was slower, and duration of action was longer for the test compds. than for THC. HU-250 exhibited cannabimimetic activity with a potency similar to THC in both species; HU-249 was 22 times less active than THC. The pattern of response rate and THC-like responding obtained with HU-249 were dissocd.; THC-like responding occurred during the later test intervals when suppression of response rate was reduced. HU-250 bound to the cannabinoid receptor with a Ki of 47.6 nM, essentially identical to that of THC. HU-249 was much less active, with a Ki of 28.3 .mu.M. The triacetate enantiomers, HU-253 and HU-254, occasioned THC-like responding in both species, HU-254 being about 4.5 times less potent than THC and 3 to 4 times more potent than HU-253. In binding, HU-253 was also less potent than HU-254. The corresponding triols were considerably more potent than the acetates; (-)-HU-256 had a Ki of 198 nM, whereas (+)-HU-255 had a Ki of 43.8 nM, comparable to that of THC.

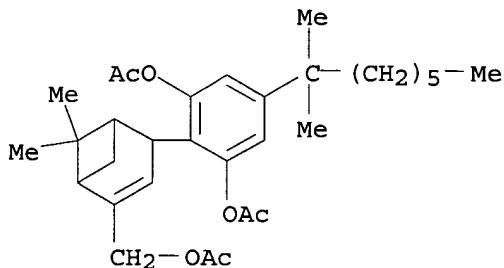
IT 76163-87-6, HU 254 76163-88-7, HU 253

RL: BIOL (Biological study)
 (cannabinoid receptor binding and tetrahydrocannabinol discriminative stimulus effect response to, structure in relation to)

RN 76163-87-6 CAPLUS

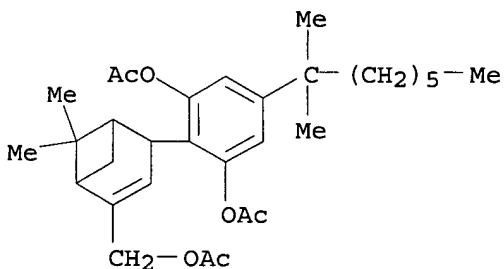
CN 1,3-Benzene diol, 2-[4-[(acetoxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1S-

(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)



RN 76163-88-7 CAPLUS

CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1R-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)



L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 1988:142840 CAPLUS

DN 108:142840

TI Structure-anticonvulsant activity relationships of cannabidiol analogs

AU Martin, Arnold R.; Consroe, Paul; Kane, Vinayak V.; Shah, Vibhakar; Singh, Vishwakarma; Lander, Naftali; Mechoulam, Raphael; Srebnik, Morris

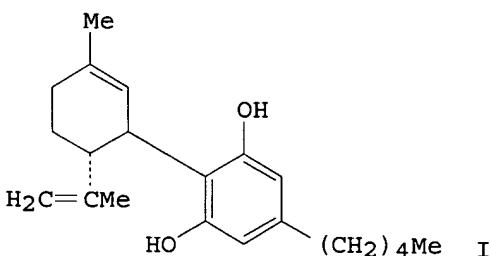
CS Coll. Pharm., Univ. Arizona, Tucson, AZ, 85721, USA

SO NIDA Res. Monogr. (1987), 79(Struct.-Act. Relat. Cannabinoids), 48-58
CODEN: MIDAD4; ISSN: 0361-8595

DT Journal

LA English

GI



AB Cannabidiol (I) exhibits anticonvulsant activity in exptl. animals and in man. As part of a structure-activity study, analogs were prepd. wherein

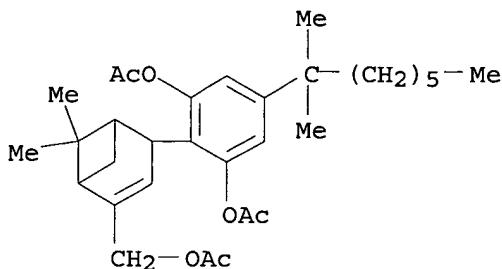
the terpene unit, the aryl unit, and/or the side chain were modified. Thus, several pinenyl and carenyl derivs., aryl ethers and acetates, and a variety of 1'',1'''-dialkylhexyl and 1'',1'''-dialkylheptyl analogs were synthesized. The compds. were evaluated for anticonvulsant activity in seizure-susceptible rats and for neurotoxicity in the rat rotorod test. Comparisons of stereoisomers of I and several analogs revealed a general lack of stereoselectivity for anticonvulsant and other central nervous system-affecting properties of this class of compds.

IT 76163-87-6P 76163-89-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and anticonvulsant activity-structure relations of)

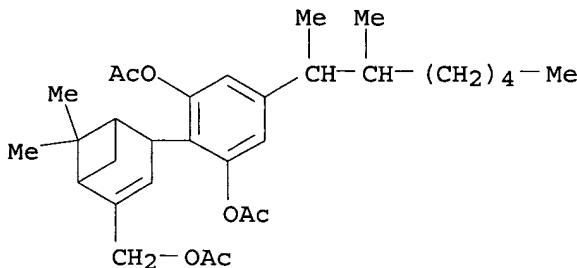
RN 76163-87-6 CAPLUS

CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1S-(1.alpha.,2.alpha.,5.alpha.)] - (9CI) (CA INDEX NAME)



RN 76163-89-8 CAPLUS

CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,2-dimethylheptyl)-, diacetate (9CI) (CA INDEX NAME)



L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 1981:480289 CAPLUS

DN 95:80289

TI Pinene derivatives, their preparation and pharmaceutical compositions comprising them

IN Mechaulam, Raphael; Lander, Naftali; Dikstein, Shabtay

PA Yissum Research and Development Co., Israel; Plantex Ltd.

SO Brit. UK Pat. Appl., 7 pp.

CODEN: BAXXDU

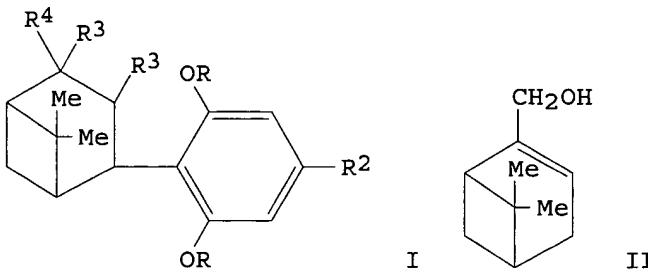
DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
PI GB 2027021	A	19800213	GB 1979-25214	19790719

GB 2027021	B2	19830427		
IL 55274	A1	19820831	IL 1978-55274	19780802
DE 2929517	A1	19800221	DE 1979-2929517	19790720
US 4282248	A	19810804	US 1979-59859	19790723
FR 2432498	A1	19800229	FR 1979-19764	19790801
FR 2432498	B1	19840921		
PRAI IL 1978-55274		19780802		
GI				

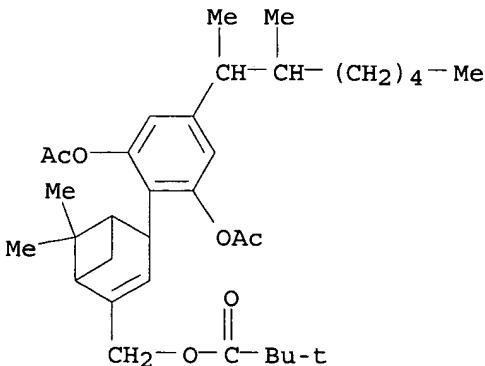


AB Pinene derivs. I [R = H, COR1 (R1 = C1-5 alkyl); R2 = Me(CH2)5CMe2, Me(CH2)4CHMeCHMe; R3 = H, R4 = Me; R32 = bond, R4 = CH2OH, CH2OR5 (R5 = C1-5 alkyl)] were prep'd. E.g., myrtenol (II) underwent sequential esterification with Me₃CCOCl, oxidn. (Na₂Cr₂O₇), redn. [LiAlH(OCMe₃)₃], reaction with 5-(1,2-dimethylheptyl)resorcinol, and acetylation to give I [R = Ac, R2 = Me(CH2)4CHMeCHMe, R32 = bond, R4 = CH₂O₂CCMe₃] (III). I are useful as analgesics; their activity was assessed by the mouse ring and tail-flick methods and by the rat foot-pressure method. ED₅₀ values for III were 25, >50, and >50 mg/kg, resp. I are also of value as central-nervous-system depressants, sedatives, tranquilizers, anticonvulsants, antimigraine agents, antiglaucoma agents, antidiarrheal agents, antiinflammatory agents, antinausea agents, and antiulcer agents.

IT 76163-92-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and analgesic properties of)

BN 76163-92-3 CAPLUS

70185-92-3 CASREG
CN Propanoic acid, 2,2-dimethyl-, [4-[2,6-bis(acetyloxy)-4-(1,2-dimethylheptyl)phenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester (9CI) (CA INDEX NAME)

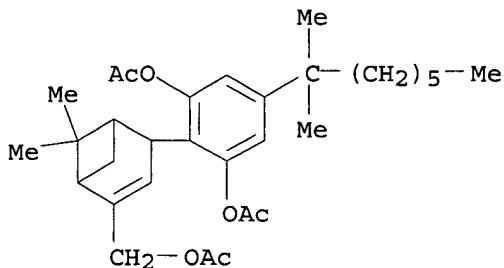


IT 76163-88-7P 76163-89-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., analgesic properties, and redn. of)

CAS ONLINE PRINTOUT 09/698,071

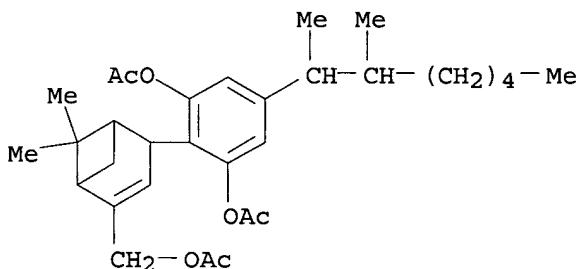
RN 76163-88-7 CAPLUS

CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1R-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)



RN 76163-89-8 CAPLUS

CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,2-dimethylheptyl)-, diacetate (9CI) (CA INDEX NAME)



L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 1981:47552 CAPLUS

DN 94:47552

TI Phenylpinene derivatives, their preparation and pharmaceutical compositions comprising them

IN Mechoulam, Raphael; Lander, Naftali; Dikstein, Shabtay

PA Yissum Research and Development Co., Israel

SO Brit. UK Pat. Appl., 7 pp.

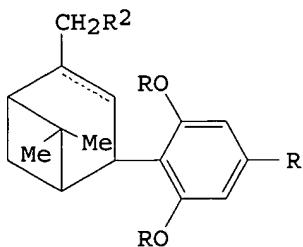
CODEN: BAXXDU

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2027021		19800213		
PRAI	IL 1978-55274		19780802		
GI					



AB The prepn. of the title compds. I (R = H, C2-6 alkanoyl; R1 = 1,1- or 1,2-dimethylheptyl; R2 = H, OH, C1-5 acyloxy) is described. Thus, (-)-I (R = Ac, R1 = 1,2-dimethylheptyl, R2 = O2CCMe3, double bond present) was prepd. from (-)-myrtenol by sequential treatment with Me3CCOCl, Na2Cr2O4, LiAlH(OCMe3)3, 5-(1,2-dimethylheptyl)resorcinol/p-MeC6H4SO3H, and Ac2O. I have analgesic, sedative, tranquilizing, central nervous system depressant, anticonvulsive, antimigraine, antiglaucoma, antinausea, antiulcer, antidiarrheal, and antiinflammatory activity. The analgesic activities of I (reported) were assessed in mice by the AcOH-induced writhing test and the tail flick test, and in rats by the foot pressure test. The central nervous system action (not reported) was tested by the mouse ring test.

IT 76163-87-6P 76163-88-7P 76163-89-8P

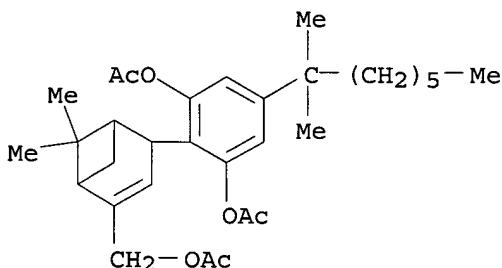
76163-90-1P 76163-91-2P 76163-92-3P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and analgesic activity of)

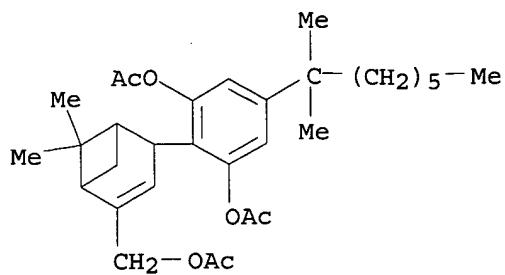
RN 76163-87-6 CAPLUS

CN 1,3-Benzene diol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1S-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)



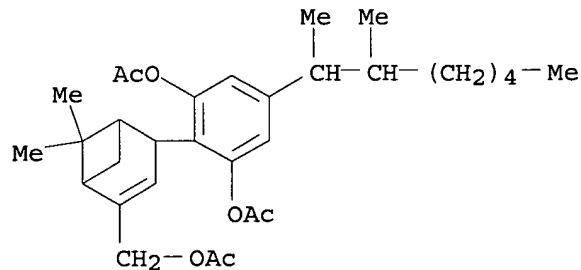
RN 76163-88-7 CAPLUS

CN 1,3-Benzene diol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1R-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)



RN 76163-89-8 CAPLUS

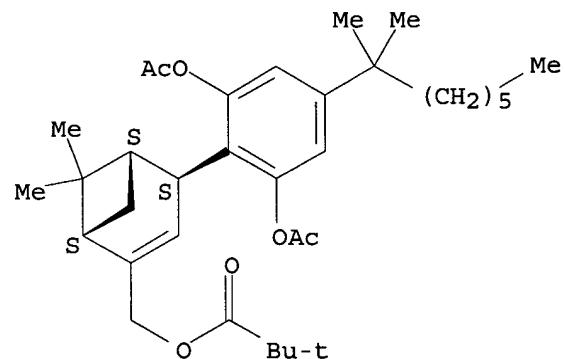
CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,2-dimethylheptyl)-, diacetate (9CI) (CA INDEX NAME)



RN 76163-90-1 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [4-[2,6-bis(acetyloxy)-4-(1,1-dimethylheptyl)phenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester, [1S-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

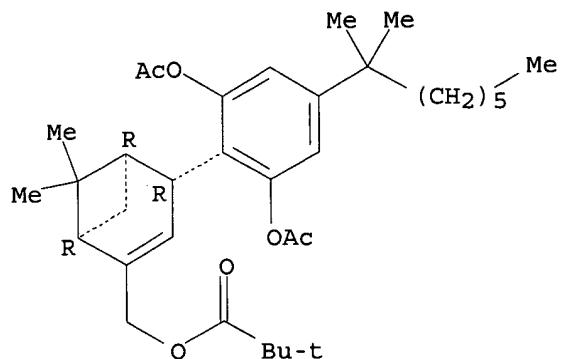
Absolute stereochemistry.



RN 76163-91-2 CAPLUS

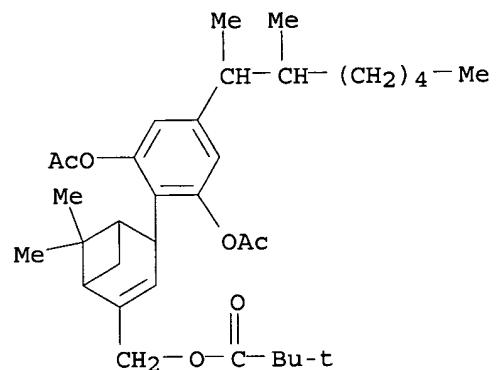
CN Propanoic acid, 2,2-dimethyl-, [4-[2,6-bis(acetyloxy)-4-(1,1-dimethylheptyl)phenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester, [1R-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 76163-92-3 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [4-[2,6-bis(acetoxy)-4-(1,2-dimethylheptyl)phenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester (9CI) (CA INDEX NAME)



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